CLAIM AMENDMENTS

1. (withdrawn) An isolated nucleic acid molecule encoding a polypeptide having GRF4 activity.

2. (withdrawn) The nucleic acid molecule of claim 1, comprising all or part of the nucleic acid molecule of [SEQ ID NO:1].

3. (withdrawn) An isolated nucleic molecule comprising at least 40% sequence identity to all or part of the nucleic acid molecule of [SEQ ID NO: 1], wherein the nucleic acid molecule encodes a polypeptide having GRF4 activity.

4. (withdrawn) The molecule of any claim 1 which is selected from a group consisting of mRNA, cDNA, sense DNA, anti-sense DNA, single-stranded DNA and double-stranded DNA.

5. (withdrawn) A nucleic acid molecule encoding the amino acid sequence of [SEQ ID NO: 2].

6. (withdrawn) A nucleic acid molecule that encodes all or part of a GRF4 polypeptide or a polypeptide having GRF4 activity, wherein the sequence hybridizes to the nucleic acid molecule of all or part of [SEQ ID NO: 1] under high stringency conditions.

7. (withdrawn) The nucleic acid molecule of claim 6, wherein the high stringency conditions comprise a wash stringency of about 0.2X SSC, about 0.1% SDS, at about 50-65°C.

8. (withdrawn) An isolated polypeptide having GRF4 activity and CDC25 domain.

9. (withdrawn) The polypeptide of claim 8, comprising all or part of the sequence of [SEQ ID NO:2].

10. (withdrawn) An isolated polypeptide comprising at least 40% sequence identity to all or part of the polypeptide of [SEQ ID NO: 2], wherein the polypeptide has GRF4 activity.

11. (withdrawn) A mimetic of the isolated polypeptide of claims 8-10, wherein the mimetic has GRF4 activity.

12. (withdrawn) A recombinant nucleic acid molecule comprising a nucleic acid molecule of any of claim 1 to claim 7 and a promoter region, operatively linked so that the promoter enhances transcription of the nucleic acid molecule in a host cell.

13. (withdrawn) A system for the expression of GRF4, comprising an expression vector and a nucleic acid molecule of any of claim 1 to claim 7 inserted in the expression vector.

14. (withdrawn) The system of claim 13, wherein the expression vector comprises a plasmid or a virus.

15. (withdrawn) A cell transferred by the expression vector of claim 14.

16. (withdrawn) A method for expressing a polypeptide comprising: transforming an expression host with an expression vector including and culturing the expression host.

17. (withdrawn) The method of claim 16, further comprising isolating the polypeptide.

18. (withdrawn) The method of claim 16 or 17, wherein the expression host is selected from the group consisting of a plant, plant cell, bacterium, yeast, fungus, protozoa, algae, animal and animal cell.

19. (withdrawn) A pharmaceutical composition, comprising all or part of the polypeptide or mimetic of any of claims 8 to 11, and a pharmaceutically acceptable carrier, auxiliary or excipient.

20. (withdrawn) A GRF4 specific antibody targeted to a region selected from the group consisting of the C-terminus, the CDC25 domain, the cNMP binding domain and the PDZ domain.

21. (withdrawn) The antibody of claim 20, wherein the antibody is a monoclonal antibody or a polyclonal antibody.

22. (withdrawn) A method of medical treatment of a disease, disorder or abnormal physical state, characterized by excessive GRF4 expression, concentration or activity, comprising administering a product that reduces or inhibits GRF4 polypeptide expression, concentration or activity.

23. (withdrawn) The method of claim 22, wherein the product is an antisense nucleic acid molecule to all or part of the nucleic acid molecule of any of claims 1 to 7, the antisense nucleic acid molecule being sufficient to reduce of inhibit GRF4 polypeptide expression.

24. (withdrawn) The method of claim 22, wherein the product comprises all or part of Nedd4.

25. (withdrawn) The method of any of claims 22-24 wherein the disease, disorder or abnormal physical state comprises cancer.

26. (withdrawn) A method of medical treatment of a disease, disorder or abnormal physical state, characterized by inadequate GRF4 expression, concentration or activity, comprising administering a product that increases GRF4 polypeptide expression, concentration or activity.

27. (withdrawn) The method of claim 26, wherein the product is a nucleic acid molecule comprising all or part of the nucleic acid molecule of any of claims 1 to 7, the DNA being sufficient to increase GRF4 polypeptide expression.

28. (withdrawn) The method of claim 27, wherein the nucleic acid molecule is administered in a pharmaceutical composition comprising a carrier and a vector operably linked to the nucleic acid molecule.

29. (currently amended) A method of identifying a compound which modulates the interaction of GRF4 with Ras, comprising

a) contacting (i) GRF4 or a portion of GRF4 selected from the group consisting of a Ras association domain and a CDC25-related GEF domain~~, a Ras-binding fragment of GRF4 or a derivative of either of the foregoing (ii),~~ with (ii) Ras ~~a GRF4-binding fragment of Ras or a derivative of either of the foregoing~~ in the presence of the compound~~; wherein (i) and (ii) are capable of binding~~; and

b) determining whether the binding between (i) and (ii) is modulated compared to a control for determining the binding of GRF4 and Ras in the absence of the compound, ~~thereby~~ wherein an increase or decrease in binding in the presence of the compound indicates ~~indicating~~ that the compound modulates the interaction of GRF4 and Ras.

30. (currently amended) A method of identifying a compound which modulates the interaction of GRF4 with Rap1, comprising

a) contacting (i) GRF4 or a portion of GRF4 selected from the group consisting of a Ras association domain ~~or~~and a CDC25-related GEF domain~~, a~~

~~Rap1-binding fragment of GRF4 or a derivative of either of the foregoing~~ with (ii) Rap1 ~~, a GRF4-binding fragment of Rap1 or a derivative of either of the foregoing~~ in the presence of the compound; ~~wherein (i) and (ii) are capable of binding;~~ and

b) determining whether the binding between (i) and (ii) is modulated compared to a control for determining the binding of GRF4 and Rap1 in the absence of the compound, wherein an increase or decrease in binding in the presence of the compound indicates ~~thereby indicating~~ that the compound modulates the interaction of GRF4 and Rap1.

31. (currently amended) A method of evaluating the cell proliferation reducing properties of a compound comprising contacting the compound with:

a) (i) GRF4, or a portion of GRF4 selected from the group consisting of a Ras association domain or a CDC25-related GEF domain~~a Ras-binding fragment of GRF4 or a derivative of either of the foregoing~~; and

b) (ii) Ras,- in the presence of the compound ~~a GRF4-binding fragment of Ras or a derivative of either of the foregoing; wherein (a) and (b) are capable of binding~~; and

c) determining whether the binding between (i) and (ii) is ~~modulated~~ inhibited compared to a control for determining the binding of GRF4 and Ras in the absence of the compound, wherein ~~an increase or decrease~~an inhibition of binding in the presence of the compound indicates~~the ability of the compound to interfere with the binding of a) with b), the ability to interfere with binding indicating~~ that the compound reduces cell proliferation.

32. (withdrawn) isolated Guanine Nucleotide Releasing Factor 4 (GRF4) polypeptide Ras activator.

33. (withdrawn) A recombinant GRF4 protein produced by a cell including a nucleic acid molecule encoding a GRF4, operably linked to a promoter.

34. (withdrawn) A Ras binding peptide comprising 10 to 100 amino acids wherein the peptide includes part of the peptide of [SEQ. ID NO.2, 4, 5 or 6] or a derivative thereof and inhibits Ras activation.

35. (withdrawn) A method of evaluating an anti-proliferation compound comprising contacting the compound with the CDC25 domain of GRF4, or a derivative thereof and determining the ability of the compound to bind to the GRF4 or derivative, wherein the ability to bind indicates that the compound inhibits cell proliferation.

36. (new) The method of claim 29, wherein the GRF4 comprises the following sequence motifs and domains, in amino to carboxyl order: a cyclic nucleotide monophosphate-binding domain, a Ras exchange motif, a PDZ association domain, a Ras association domain, a CDC25-related GEF domain, a first PY motif, a second PY motif, and a COOH-terminal SaV sequence conforming to a PDZ binding motif.

37. (new) The method of claim 29, wherein the GRF4 comprises SEQ ID NO:2 or a sequence of at least 80% sequence identity to SEQ ID NO:2.

38. (new) The method of claim 30, wherein the GRF4 comprises the following sequence motifs and domains, in amino to carboxyl order: a cyclic nucleotide monophosphate-binding domain, a Ras exchange motif, a PDZ association domain, a Ras association domain, a CDC25-related GEF domain, a first PY motif, a second PY motif, and a COOH-terminal SaV sequence conforming to a PDZ binding motif.

39. (new) The method of claim 30, wherein the GRF4 comprises SEQ ID NO:2 or a sequence of at least 80% sequence identity to SEQ ID NO:2.

40. (new) The method of claim 31, wherein the GRF4 comprises the following sequence motifs and domains, in amino to carboxyl order: a cyclic nucleotide monophosphate-binding domain, a Ras exchange motif, a PDZ association domain, a Ras association domain, a CDC25-related GEF domain, a first PY motif, a second PY motif, and a COOH-terminal SaV sequence conforming to a PDZ binding motif.

41. (new)The method of claim 31, wherein the GRF4 comprises SEQ ID NO:2 or a sequence of at least 80% sequence identity to SEQ ID NO:2.